Anthos Therapeutics Launches Second Phase 3 Clinical Trial of Its Dual-acting Factor XI Inhibitor, Abelacimab

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Anthos Therapeutics →
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Abelacimab is the only Factor XI inhibitor currently being evaluated in Phase 3 trials

The MAGNOLIA study will compare abelacimab against the current standard of care for VTE in cancer associated thrombosis (CAT) in patients with GI/GU cancers

Enrolling ~2700 patients, the company's robust Phase 3 clinical trial program for CAT consists of the MAGNOLIA and ASTER studies

CAMBRIDGE, Mass., August 25, 2022 -- Anthos Therapeutics, a clinical-stage biopharma company developing innovative therapies for cardiovascular and metabolic diseases, today announced the initiation of recruitment for its second Phase 3 clinical trial investigating abelacimab, its novel dual-acting fully human monoclonal antibody targeting both Factor XI and Factor XIa. The MAGNOLIA study is recruiting patients who are at risk of thrombosis and diagnosed with gastrointestinal/genitourinary (GI/GU) cancers, which are cancers known to have a higher risk of bleeding than other cancers[1]. The study is one of two complementary, international, multicenter trials where abelacimab is being studied in patients with cancer associated thrombosis (CAT), a condition for which there is an unmet need as currently available anticoagulants have

been associated with an increased risk of bleeding[2,3]. In the MAGNOLIA trial, monthly treatment with abelacimab is being compared with once daily injection of dalteparin, the current anticoagulant standard of care in patients with GI/GU cancers, to assess the effects on venous thromboembolism (VTE) recurrence and bleeding in patients with cancer associated VTE, a leading cause of death in patients with cancer[4].

“Based on the positive Phase 2 data we’ve seen to date, we are hopeful that this trial will validate the promise of abelacimab as a much-needed new treatment option for this high-risk and difficult-to-treat patient population. With a 20-fold increase in risk of CAT in GI cancers compared to patients without cancer, we are particularly pleased that abelacimab is being explored to reduce VTE recurrence and bleeding in GI and GU cancers,” said Alok A. Khorana, M.D., Professor of Medicine, Cleveland Clinic Lerner College of Medicine, Case Western Reserve University and member of the Abelacimab CAT Program Steering Committee. “Because cancer patients who receive current anticoagulant treatment to manage VTE have a higher bleeding risk than patients without cancer receiving anticoagulants[5], it’s too often that physicians are forced to choose between preventing life-threatening clots, and putting their patients at risk of uncontrolled bleeding, particularly in patients with GI/GU cancers.”

The head-to-head design of this trial will provide critical information concerning the efficacy of this novel therapeutic in addressing VTE and bleeding, a devastating and unpredictable complication of cancer that can significantly impact a patient’s quality of life. Abelacimab is a dual-acting fully human monoclonal antibody targeting both Factor XI and Factor XIa with high affinity and selectivity. It has the potential to achieve hemostasis-sparing anticoagulation: effective protection from thromboembolic events with a reduced risk of clinically significant bleeding compared to existing therapies. Moreover, the once-monthly dosing profile may reduce the burden of a daily regimen for patients who are already traveling to the clinic to receive multiple therapies for their cancer care.

“Unfortunately, many patients at risk of thrombosis stop taking low molecular weight heparins, which require daily injections, after less than 2 months, and sadly patients don’t stay much longer on DOACs[6]. Our hope is that the monthly dosing schedule of abelacimab and its potential enhanced safety profile will play a role in improving adherence and quality of life,” added Dr. Khorana.

Scientific evidence suggests that abelacimab, which takes aim at an entirely new target, Factor XI (and its activated counterpart Factor XIa), could enable pharmacological ‘uncoupling’ of the physiological hemostasis and pathological thrombosis pathways. This approach would enable patients to achieve the delicate balance between the clotting necessary to prevent uncontrolled bleeding while being protected from life-threatening blood clots.

Venous thromboembolism (VTE), which includes both deep vein thrombosis and pulmonary embolism, is the second most prevalent cause of death in patients with cancer, second only to the disease itself[7]. VTE affects an estimated 300,000-600,000 individuals in the U.S. each year, causing considerable morbidity and mortality. It is a disorder that can occur in all races and ethnicities, all age groups, and both genders. However, treatment of CAT in particular can be challenging because the currently available anticoagulants used to treat VTE have been associated with an increased risk of bleeding[8,9]. This risk remains a strong deterrent to optimal prescribing of these products in routine practice.

"Solving this life-or-death dilemma faced by the oncology community is a priority at Anthos. The urgent need for this research and the development of effective and safer anticoagulants is underscored not only by the FDA’s recent fast track designation of abelacimab [for the treatment of thrombosis associated with cancer], but also by the passion and commitment of our CAT Scientific Steering Committee to the patients they treat,” said Dan Bloomfield, M.D., Chief Medical Officer, Anthos Therapeutics.

“The data provided by the CAT Phase 3 program, in addition to our ongoing Phase 2 AZALEA-TIMI 71 trial comparing abelacimab to rivaroxaban in atrial fibrillation (AF), will help to shed light on the role of abelacimab in managing this complex issue not only in the treatment of cancer but also in other challenging therapeutic areas,” added Dr. Bloomfield.

About the Abelacimab Phase 3 Program in Cancer Associated Thrombosis (CAT)
The abelacimab Phase 3 CAT program comprises two complementary studies targeting to enroll approximately 2700 patients across 220 sites in more than 20 countries -- the largest program of any anticoagulant performed in cancer-associated thrombosis.

MAGNOLIA is an international multicenter, randomized, open-label, blinded endpoint evaluation, Phase 3 study in patients with gastrointestinal (GI) / genitourinary (GU) cancer in whom DOAC treatment is not recommended. The study will compare the effect of abelacimab relative to dalteparin on VTE recurrence and bleeding in patients with cancer associated VTE who are at a high bleeding risk with non-resectable, locally or regionally invasive GI / GU tumors. Abelacimab 150 mg will be administered intravenously (IV) on Day 1 and subcutaneously (SC) monthly thereafter for up to 6 months; dalteparin administered subcutaneously will be given daily, 200 IU/kg/day for the first month, and then 150 IU/kg/day up to 6 months. Recruitment for this trial began in August 2022.

ASTER is an international multicenter, randomized, open-label, blinded endpoint evaluation, Phase 3 study comparing the effect of abelacimab relative to apixaban on venous thromboembolism (VTE) recurrence and bleeding in patients with cancer associated VTE in whom DOAC treatment is recommended. Abelacimab 150 mg will be administered intravenously (IV) on Day 1 and subcutaneously (SC) monthly thereafter for up to 6 months; Apixaban 10 mg will be administered orally, twice daily (bid) for the first 7 days, followed by 5 mg bid up to 6 months.

About the AZALEA-TIMI 71 Phase 2 Trial

The AZALEA-TIMI 71 trial is an event-driven, randomized, active-controlled, blinded endpoint, parallel-group study to evaluate the effect of two blinded doses of abelacimab relative to open label rivaroxaban on the rate of major or clinically relevant non-major (CRNM) bleeding events in patients with atrial fibrillation (AF) who are at moderate-to-high risk of stroke. The trial completed enrollment in December 2021, with 1287 patients across 95 global study sites including the U.S., Canada, as well as from parts of Europe, and Asia.

About Abelacimab

Abelacimab is a novel, highly selective, fully human monoclonal antibody designed to induce effective hemostasis-sparing anticoagulation through Factor XI inhibition. Abelacimab targets the active domain of Factor XI, demonstrating dual inhibitory activity against both Factor XI and its activated form, Factor XIa. Abelacimab can be administered intravenously (IV) to achieve rapid inhibition of Factor XI activity and then used subcutaneously (SC) monthly to maintain nearly complete inhibition in a chronic setting. In a PK/PD study, abelacimab administered IV provided profound suppression of Factor XI within one hour after the start of therapy and maintained near maximal inhibition for up to 30 days.[10,11] In a Phase 2 study whose results were published in the *New England Journal of Medicine* in 2021, a single intravenous dose of abelacimab after knee surgery reduced the rate of venous thromboembolism by 80%, measured 10 days after surgery, compared to enoxaparin.[4,] Factor XI inhibition offers the promise of hemostasis-sparing anticoagulation for the prevention and treatment of arterial and venous thromboembolic events.[12] Abelacimab, an investigational agent that has not been approved for any indication, received FDA Fast Track Designation in July 2022 for the treatment of thrombosis associated with cancer.

About Anthos Therapeutics

Anthos Therapeutics is a clinical-stage biopharmaceutical company focused on the development and commercialization of genetically and pharmacologically validated innovative therapies to advance care for people living with cardiovascular and metabolic (CVM) diseases. Anthos Therapeutics aims to combine the agility of a biotech with the

rigor of a large pharmaceutical company. Anthos Therapeutics was launched by Blackstone Life Sciences in 2019. For more information, visit the company's website and follow on Twitter and LinkedIn.

Forward Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the initiation, and timing, of future clinical trials and its research and development. All statements, other than statements of historical facts, contained in this press release, including statements regarding the company's strategy, future operations, future financial position, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "become", "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. In addition, the forward-looking statements included in this press release represent the company's views as of the date hereof and should not be relied upon as representing the company's views as of any date subsequent to the date hereof. The company anticipates that subsequent events and developments will cause the company's views to change. However, while the company may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so.

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